



Refractory Hypoglycemia From Hepatocellular Carcinoma: How Low Can You Go?

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Introduction

- Severe, refractory hypoglycemia is a rare paraneoplastic manifestation of hepatocellular carcinoma (HCC) with poor prognosis
- We present a patient with hypoglycemia as an initial presentation of HCC

Case Presentation

- 68-year-old man presented with syncope and altered mental status
- Past Medical History:** decompensated Child-Pugh class B hepatitis C cirrhosis with sustained virologic response after treatment
- Magnetic Resonance Imaging (MRI):** 22 centimeter multi-focal metastatic HCC to bone and lung (Figure 1)
- Labs:** low insulin, low c-peptide, low insulin-like growth factor-1 (IGF-1), normal insulin-like growth factor-2 (IGF-2), high IGF-2/IGF-1 ratio confirmed non-islet cell tumor hypoglycemia (Table 1)
- Management:** tumor debulking with transarterial bland embolization (TAE); Endocrinology consult recommending intravenous dextrose (50% pushes as needed, 10% continuous infusion), intramuscular glucagon, dexamethasone, and frequent feeding
- Clinical Course:** persistent hypoglycemia with new-onset seizures

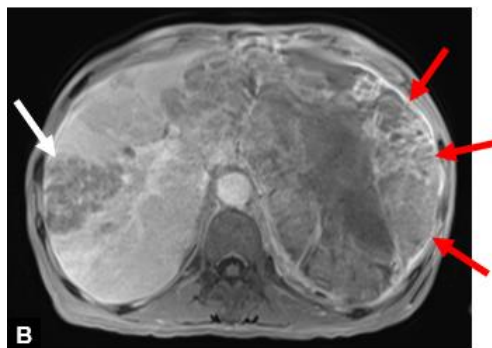
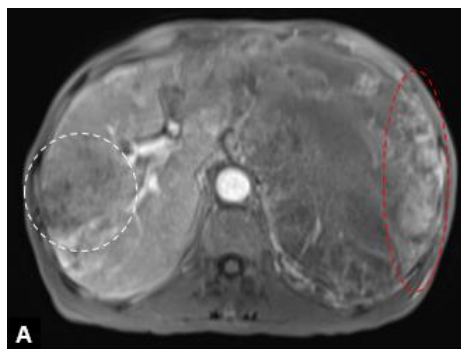


Figure 1. MRI abdomen shows large hepatic mass with mosaic architecture replacing the left lobe. Foci of (A) arterial phase hyperenhancement (APHE) along its left periphery (red dotted oval) demonstrates corresponding washout in (B) delayed phase (red arrows). Smaller right hepatic mass also demonstrates APHE (white dotted circle) and washout (white arrow).

Lab	Value	Reference Range
Glucose (mg/dL)	12	70-121
C-peptide (ng/mL)	0.26	0.80-3.85
Insulin (uIU/mL)	<0.1	2.0-19.6
IGF-1 (ng/mL)	12	41-279
IGF-2 (ng/mL)	392	267-616
IGF-2/IGF-1 ratio	32.7	<10

Table 1. Laboratory values

Case Presentation (Cont.)

- Management (Cont.):** history of TAE limited further locoregional therapy (LRT) options; Oncology consult considered Sorafenib
- Clinical Course (Cont.):** patient opted for comfort-directed care and died one month after admission

Discussion

- Two types of HCC-induced hypoglycemia exist. Type A is mild, occurs in rapidly-growing tumors, and mortality may occur within weeks. It is caused by the inability of a tumor-ridden liver to meet the body's glucose demand. Type B is severe, occurs with slowly-growing tumors, and mortality may occur within a year. It is caused by defective processing of the IGF-2 precursor by tumor cells, resulting in increased glucose uptake.
- The most effective management is cytoreduction by surgery, chemotherapy and LRT
- Pharmacologic options including steroids, frequent feeding, dextrose, glucagon and growth hormone have mixed results
- Patients with cirrhosis and hypoglycemia should be screened for HCC as this may be a presenting symptom